

APPLN. FILING DATE: JUNE 10, 1988
TIT: PRECOMBINANT IMMUNOGLOBULI
PRECORATIONS

INVENTOR(S): CABILLY ET AL. APPLICATION SERIAL NO: 07/205,419

SHEET 1 of 19

6331415

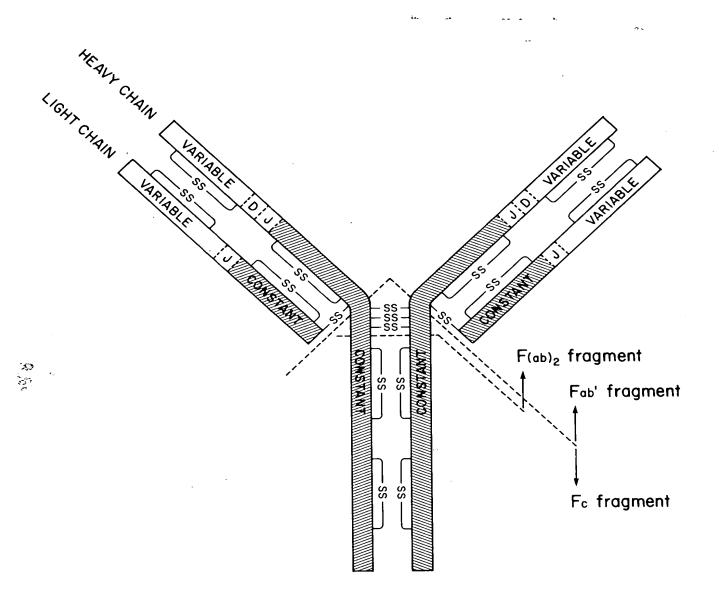


Fig.1.

APPLN. FILING DATE: JUNE 10, 1988
TITE RECOMBINANT IMMUNOGLOBUL PRESERVATIONS

INVENTOR(S): CABILLY ET AL.
APPLICATION SERIAL NO: 07/205,419

SHEET 2 of 19

TGTGATG ACACTAC ATAGTTG ATAGTTG GTCTAAA GTCGAC GTTCGAC	haelli AGTCTC ACAAATTCAT GTCCACATCA GTAGGAGACA GGGTCAGCAT CACCTGCAAG TCAGAG TGTTTAAGTA CAGGTGTAGT CATCCTCTGT CCCAGTCGTA GTGGACGTTC ·	SCFI ecorii hpaii hpaii hofi AGAAACCAGG ACAATCTCCT AAACTACTGA TTTACTGGGC ATCCACCGG CACACTGAG TCTTTGGTCC TGTTAGAGGA TTTGATGACT AAATGACCCG TAGGTGGCC GTGTGACCTC	hphi Ctcacc attagcaatg tgcagtctga tgacttggca gattatttct gtcaacaata gagtgg taatcgttac acgtcagact actgaaccgt ctaataaaga cagttgttat	fnu4HI alui sfaNi bbv GAGCTGAAAC GGGCTGATGC TGCACCACT GTATCCATCT TCCCACCATC CAGTGAGCAG CTCGACTTTG CCCGACTACG ACGTGGTTGA CATAGGTAGA AGGGTGGTAG GTCACTCGTC foki	mboli ACTICTACCC CAAAGACATC AATGICAAGI GGAAGATIGA IGGCAGIGAA CGACAAAATG
	GTTGCTGTGG TTGTCTGGTG TTGAAGGAGA CATTGTGA) Caacgacacc aacagaccac aacttcctct gtaacact/	fnu4HI scrFI bby ecoRII GCCAGTCAGG ATGTGGGTGC TGCTATAGCC TGGTATCA/ CGGTCAGTCC TACACCCACG ACGATATCGG ACCATAGTI	A A A C	sau96 avall alu T TCGGTGCTGG GACCAAGC A AGCCACGACC CTGGTTCG/	mnll ddel xmn
	.	101	201	301	401

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TITLE ECOMBINANT IMMUNOGLOBULIN PREPARATIONS

INVENTOR(S): CABILLY ET AL.
APPLICATION SERIAL NO: 07/205,419

SHEET 3 of 19

501	fnu4HI hgal GCGTCCTGAA CAGTTGGACT GATCAGGACA GCAAAGACAG CACCTACAGC ATGAGCAGCA CCCTCACGTT GACCAAGGAC GAGTATGAAC GACATAACAG CGCAGGACTT GTCAACCTGA CTAGTCCTGT CGTTTCTGTC GTGGATGTCG TACTCGTCGT GGGAGTGCAA CTGGTTCCTG CTCATACTTG CTGTATTGTC	
601	mnlI haeIII haeI CTATACCTGT GAGGCCACTC ACAAGACATC AACTTCACCC ATTGTCAAGA GCTTCAACAG GAATGAGTGT TAGAGACAAA GGTCCTGAGA CGCCACCACC GATATGGACA CTCCGGTGAG TGTTGTGAAGTGGG TAACAGTTCT CGAAGTTGTC CTTACTCACA ATCTCTGTTT CCAGGACTCT GCGGTGGTGG	
701	alul alul hgiA mnll mnll mnll Adel mnll mnll hgiA mnll AGCTCCCCAG CTACCACTGT TGCGGTGCTC CAAACCTCT CCCCACCTCC TCGAGGGGTG GAGGGTGCTC CAAACCTCCT CCCACCTCC TCGAGGGGTG GAGGGTAGGGT	
801	mnli mnli mnli TTCTCCTCCT CCTCCCTTTC CTTGGCTTTT ATCATGCTAA TATTTGCAGA AAATATTCAA TAAAGTGAGT CTTTGCACTT GA AAGAGGAGGA GGAGGGAAAG GAACCGAAAA TAGTACGATT ATAAACGTCT TTTATAAGTT ATTTCACTCA GAAACGTGAA CT	

nucleotides: 882

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TITLE ECOMBINANT IMMUNOGLOBULIN
PREPARATIONS :
INVENTOR(S): CABILLY ET AL.
APPLICATION SERIAL NO: 07/205,419
SHOW

SHEET 4 of 19

20 ser AGC	50 trp UGG	80 ser ucu	110 asp GAU	140 tyr UAC	170 asp GAC	200 thr ACA	AGACAAAGGUCCUGAGACGCCACCÀCCAGCUCCCAGCUCCAUCCUAUCUUCCCUUCUAA	<u> GUGCUCCAAACCUCCUCCCACCUCCUUCUCCUCCUCCUUCCCUUCCUUGGCUUUUAUCAUGCUAAUAUUUGCAGAAAA</u>
val GUC	tyr UAC	gln CAG	ala GCU	phe uuc	1 y s A A A	lys AAG	າກວວເ	IGCAG
arg AGG	ile Auu	va] GUG	a CGG	asn AAC	ser AGC	glu ala thr his lys GAG GCC ACU CAC AAG	וכחתם	AUUL
asp GAC	Jeu CUG	asn AAU	1 y s A A A	asn AAC	a s p GAC	thr ACU	CUAL	UAAU
val gly GUA GGA	leu leu CUA CUG	ser AGC	leu CUG	leu UUG	g]n CAG	ala GCC	CAUC	AUGC
val GUA	lys AAA	ile AUU	D A G	phe UUC	asp GAU	g d G A G	νεςυς	UAU
ser UCA	pro	u thr i	leu CUG	cys UGC	thr ACU	cys UGU	/222	າດຄວ
ser thr UCC ACA	ser ucu	thr leu ACU CUC	thr lys ACC AAG	va] GUG	ser trp AGU UGG	thr	ופכתנ	ານທີ່ເ
ser UCC	gln CAA	thr ACU	thr ACC	val GUC	ser AGU	tyr UAU	, ACCA	DOROL
met AUG	gly GGA	phe uuc	91y 666	ser val val UCA GUC GUG	asn AAC	ser AGC	CACC	าวววเ
10 phe UUC	40 pro ccA	70 asp GAU	100 ala GCU	130 ala GCC	160 leu CUG	190 asn ser tyr thr c AAC AGC UAU ACC U	ACGC	າວວກ:
1 y s A A A	lys AAA	thr ACA	91y 66U	91y GGU	val GUC	glu tyr glu arg his GAG UAU GAA CGA CAU	UGAG	וכתכנ
ser his ucu cac	gln gln CAA CAG	ser gly ucu GGG	p he UUC	ser gly ucu GGA	asn gly AAU GGC	arg CGA	ວວກອະ	וחכחנ
ser ucu	gln CAA	ser ucu	thr ACG	ser UCU	asn AAU	glu GAA	AAAG	າວວກ:
thr gln s ACC CAG	tyr UAU	ser gly AGU GGA	pro leu CCU CUC	thr ACA	gln CAA	tyr UAU		CAC
thr ACC	trp UGG	ser AGU	pro	leu UUA	arg CGA	g]u GAG	AM UAG) ວວກເ
met AUG	ala GCC	91y 66c	tyr UAU	gln leu CAG UUA	g]u GAA	a sp GAC	214 cys ugu	נכתכנ
val GUG	ile AUA	thr ACA	91y 666	g]u GAG	ser AGU	1ys AAG	glu GAG	SAAA(
ile AUU	ala GCU	phe UUC	ser AGC	ser AGU	91y 66c	thr ACC	asn AAU	ງວກວະ
asp GAC	ala GCU	arg CGC	tyr UAU	ser UCC	asp GAU	leu UUG	a rg AGG	าธอบ
91y 66A	30 gly GGU	60 asp GAU	90 gln CAA	120 pro CCA	150 11e AUU	180 thr ACG	210 asn AAC	3006
leu trp leu ser gly val glu CUG UGG UUG UCU GGU GAA	va] GUG	oro CCU	gln CAA	pro CCA	lys AAG	leu CUC	phe UUC	CACU(
val GUU	asp GAU	val GUC	cys UGU	phe uuc	trp UGG	thr	ser AGC	:UAC
91y 66U	gln CAG	91y 66A	p he uuc	ile Auc	1 y s A A G	ser AGC	1ys AAG	CGAC(
ser UCU	ser AGU	thr ACU	tyr UAU	ser	val GUC	ser AGC	pro ile val CCC AUU GUC	CAAG
leu UUG	ala GCC	his CAC	a s p G A U	thr val Acu GUA	asn AAU	met AUG	ile AUU	CCCA(
trp UGG	lys AAG	arg CGG	ala GCA	thr	11e AUC	ser AGC	0 T O))))
	cys UGC	thr	leu UUG	Pro	asp fle	tyr UAC	ser	<u> </u>
-9 1eu 006	thr ACC	ser UCC	asp GAC	ala GCA	1 y s A A A	thr Acc	thr	ວນນຣ(
9	11e AUC	ala GCA	asp GAU	ala GCU	0 0 0 0 0	ser AGC	ser UCA	000

UAUUCAAUAAAGUGAGUCUUUGCACUUGA

APPROVED O.G. FIG. CLASS SUBCLASS БÝ DRAFTSMAN

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INVENTOR(S): CABILLY ET AL.

APPLICATION SERIAL NO: 07/205,419

SHEET 5 of 19

	hinfl GAGTCAGCAC CTCAGTCGTG	sau96 avaII TGAACACGGA CC ACTTGTGCCT GC	sau96 hinfl GAGTCAGCAC TGAACACGGA CCCTCACGA TGAACTTCGG GCTCAGCTTG ATTTACCTTG TCCTTGTTTT AAAAGTTGTC CAGTGTGAAG TGATGCTGGT CTCAGTCGTG ACTTGTGCCT GGGGAGTGCT ACTTGAAGC CGAGTCGAAC TAAATGGAAC AGGAACAAAA TTTTCAACAG GTCACACTTC ACTACGACCA	TGAACTTCGG ACTTGAAGCC	ddel alul alul GCTCAGCTTG CGAGTCGAAC	ATTTACCTTG TAAATGGAAC	aha] TCCTTGTTTT AGGAACAAAA	III AAAAGTTGTC TTTTCAACAG	S FANI CAGTGTGAAG GTCACACTTC	TGATGCTGGT ACTACGACCA
101	hinfl GGAGTCTGGG CCTCAGACCC	hinfI GGAGTCTTAA CCTCAGAATT	scrFI sau96 mnl1 GGAGTCTGGG GGAGTCTTAA TGGAGCCTGG AGGTCCTG AAACTCTCCT GTGCAGCCTC TGGATTCACT TTCAGTAGAT ATGCCATGTC TTGGGTTCGC CCTCAGACCC CCTCAGAATT ACCTCGGACC TCCCAGGGAC TTTGAGAGGA CACGTCGGAG ACCTAAGTGA AAGTCATCTA TACGGTACAG AACCCAAGCG	rFI sau96 mnli oRII: avall TGG AGGTCCCTG	AAACTCTCCT TTTGAGAGGA	fnu4HI bbv mnlI GTGCAGCCTC CACGTCGGAG	hinfI TGGATTCACT ACCTAAGTGA	TTCAGTAGAT AAGTCATCTA	ATGCCATGTC TACGGTACAG	TTGGGTTCGC AACCCAAGCG
201	hinfi CAGACTCCGG AC GTCTGAGGCC TC	I mnlI mbolI AGAAGGCT TCTTCCGA	hpall mnll hinfl mboll CAGACTCCGG AGAAGAGGCT GGAGTGGGTC GCAACCATTA GTAGTGGTGG GTCTGAGGCC TCTTCTCCGA CCTCACCCAG CGTTGGTAAT CATCACCACC	GCAACCATTA	GTAGTGGTGG CATCACCACC	TAGTTCACAC ATCAAGTGTG fok!	CTTCCATCCA Gaaggtaggt	hphi Tagticacac cticcatcca gacagigtga agggcgatic accatcicca Atcagigtg gaaggtaggt ctgtcacact tcccgctaag iggtagaggt	hph hinfl Agggcgattc TCCGCTAAG	ıI Accatctcca Tggtagaggt
301	GAGACAATGC CTCTGTTACG	CAAGAACACC GTTCTTGTGG	mnli mnli ddel ddelli GAGACAATGC CAAGAACACC CTGTACCTGC AAATGAGCAG TCTGAGGTCT GAGGACACGG CCATGTATTA CTGTGCAAGA CCCCCTCTTA TTTCGTTAGT CTCTGTTACG GTTCTTGTGG GACATGGACG TTTACTCGTC AGACTCCAGA CTCCTGTGCC GGTACATAAT GACACGTTCT GGGGGAGAAT AAAGCAATCA	AAATGAGCAG TTTACTCGTC	mnll mnll ddel ddel TCTGAGGTCT GAGG AGACTCCAGA CTCC	mnll el GAGGACACGG CTCCTGTGCC	III CCATGTATTA GGTACATAAT	CTGTGCAAGA GacacGttct	mnll CCCCCTCTTA GGGGGAGAAT	TTTCGTTAGT AAAGCAATCA
. 401	AGCGGACTAT	GCTATGGACT	xholl scrfl sau34 mnll mnll mnll ddel ecoRill dpnl ddel bphl ddel bpnl benefecteat cctcaccc ccatctett accecaet teccteat ccataccte teached benefected benefeted	mnlI ddeI AGGAACCTCA TCCTTGGAGT	hphI GTCACCGTCT CAGTGGCAGA	mnll ddel cctcagccaa ggagtcggtt	AACGACACCC TTGCTGTGGG	CCATCTGTCT GGTAGACAGA	sau9 hae1 ATCCACTGGC TAGGTGACG	xholl scrfl sau96 sau3A ecoRll haelll dpnl TGGC CCCTGGATCT

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APPLN. FILING DATE: JUNE 10, 1988
TITLE RECOMBINANT IMMUNOGLOBULIN
PREPARATIONS
INVENTOR(S): CABILLY ET AL.
APPLICATION SERIAL NO: 07/205,419
SHOW

SHEET 6 of 19

APPROVED O.G. FIG. ВY DRAFTSMAN

APPLN. FILING DATE: JUNE 10, 1988
TITLE: COMBINANT IMMUNOGLOBULIN
PREPARATIONS
INVENTOR(S): CABILLY ET AL.
APPLICATION SERIAL NO: 07/205,419
SH

SHEET 7 of 19

APPROVED O.G. FIG. CLASS SUBCLASS БÝ DRAFTSMAN

APPLN. FILING DATE: JUNE 10, 1988 TIT RECOMBINANT IMMUNOGLOBUL PREARTIONS

INVENTOR(S): CABILLY ET AL.

APPLICATION SERIAL No: 07/205,419

SHEET 8 of 19

1 glu GAA	a rg AGA	ser UCC	thr ACG	val GUC	leu CUG	gln CAG	ala GCC	phe
cy s ugu	30 ser AGU	60 Pro CCA	90 asp GAC	120 thr ACC	150 cys UGC	180 1eu CUG	210 pro cc6	240 val GUC
gln CAG	phe UUC	leu Cuu	g]u GAG	val GUC	91y 66A			ser ucu
val GUC	thr ACU	h1s, CAC	ser ucu	ser UCA	Jeu CUG	ala GCU	a 1 a GCC	ser UCA
val GUU	p he UUC	ser UCA	a rg AGG	thr ACC	thr	CCA OA	val GUU	val. GUA
1ys AAA	91y GGA	ser AGU	leu CUG	91y GGA			asn AAC	g]u GAA
]eu uuA	ser	91y 660	ser AGU	gln CAA	met AUG	thr	cys UGC	Pro CCA
va] GUU	a]a 000							
leu CUG	ala GCA			trp UGG	ASD	val GUG	val GUC	
val GUC	cys UGU	ser AGU	gln CAA	tyr UAC	thr ACU	91y 66U	thr ACC	cys UGU
-10 leu	se. UCC	11e Auu	leu CUG	a s p G A C	gln CAA	ser AGC	g]u GAG	11e AUA
tyr UAC	20 1eu CUC	50 thr Acc	80 tyr UAC	110 met AUG	140 ala GCC	170 ser UCC	200 ser AGC	230 cys UGC
fle AUU	lys AAA	ala GCA	leu CUG	ala GCU	ala GCU	leu CUG	010	pro
leu UUG	leu CUG			tyr UAU				
ser	ser UCC	trp UGG					pro	
leu CUC	91y 666	g 1 u G A G	1ys AAG		pro CCU	ser ucu	ser AGC	91y GGU
91y 666	91y 66A	leu CUG		val GUA	a 1 a GCC	asn AAC	ser	cys UGU
phe UUC	pro	arg AGG	AAU			trp UGG	Pro CCC	asp GAU
asn AAC	glu GAG						val GUC	arg AGG
met AUG	met AUG		arg AGA					മഠ
CACG	leu UUA	010 000	ser UCC	leu CUU	val GUC	thr ACA	va] GUG	va] GUG
GAGUCAGCACUGAACACGGACCCCUCACG	10 val GUC	40 thr ACU	70 11e AUC	100 Pro CCU	130 ser UCU	160 val GUG	190 ser UCA	220 11e AUU
GGAC	gly GGA	gln CAG	thr	010	Pro	Pro	ser AGC	lys lys AAG AAA
ACAC	9] y 666	arg CGC	phe uuc	arg AGA	9 2 2 2	g]u GAG	ser AGC	lys AAG
CUGA	ser	val GUU	a G G A	ala GCA	thr	pro	leu CUG	asp GAC
AGCA	g l u GAG	trp UGG	glu gly d GAA GGG	cys ugu	lys thr AAA ACG	tyr phe UAU UUC	thr ACU	va] GUG
AGUC	val GUG	ser ucu	g 1 u GAA	tyr UAC	1ys AAA	tyr UAU	tyr UAC	lys AAG
9	leu CUG	met AUG	cys UGU	ty r UAU	a]a GCC	9 3 y 66 C	leu	thr lys val a
	met AUG	ala GCC	gln CAG	met AUG	ser UCA	1ys AAG	a s p G A C	Ser
•	val GUG	tyr UAU	arg Aga	ala GCC	ser UCC	val GUC	ser UCU	ser AGC



APPLN. FILING DATE: JUNE 10, 1988
TITLE: COMBINANT IMMUNOGLOBULIN
PREPARATIONS
INVENTOR(S): CABILLY ET AL.
APPLICATION SERIAL NO: 07/205,419
SHIP



SHEET 9 of 19

						_	
pro 000	arg CGC	010	asp GAU	tyr UAC	asn AAU	ກວວກ	
270 asp GAU	300 phe uuc	330 ala GCC	360 1 y s A A G	390 asn AAC	420 gly GGA	UCCCAGUGUCCU	
asp GAU	thr ACU	oro CCU	ala GCC	glu GAG	ala GCA	ວວວກ	
lys AAG	ser AGC	phe UUC	e t UG	1 a	g]u GAG	OP UGA	
e r AGC	asn AAC	ala phe GCU UUC	o pro pro lys glu gln m a CCU CCC AAG GAG CAG A	Pro	trp UGG	447 1ys AAA	
asp ile s GAC AUC /	p he UUC	ala GCA	glu GAG	gln CAG		91y GGU	
asp GAC	gln CAG	ser AGU	1 y s A A G	91y 666	ser AGC	pro CCU	
va] GUA	glu GAG	asn AAC	pro CCC	asn AAU	lys AAG	ser pro UCU CCU	
val GUG	g]u GAG	val asn GUC AAC	pro	n trp asn gly G UGG AAU GGG	val gin lys ser asn GUG CAG AAG AGC AAC	h i s CAC	AA
val GUU	arg CGG	arg AGG	7 2 2 2 3	g]ı	val GUG	ser his UCC CAC	GAAA
cys UGU	0 r 0	cys UGC	ile AUU	trp UGG	asn AAU	Jen	0000
260 thr ACG	290 gln CAA	320 1ys AAA	350 thr ACC	380 91u GAG		440 ser AGC	00900
val GUC	thr ACG	glu phe GAG UUC	tyr UAC	val GUG	lys AAG	lys AAG	16CAC
o lys va tu AAG GU	gln CAG	91 u GAG	val GUG	thr ACU	ser AGC	91 u GAG	70001
0 0 0 0	ala GCU	λ. Α.	gln	. − ∀	+> ⊃	his thr glu lys CAU ACU GAG AAG	AGC/
thr ACU	thr ACA	n gly 1 U GGC A	pro	asp GAC	val GUC	his CAU	AUA/
leu CUG	his CAC	asn AAU	ala GCU	glu GAA	phe UUC	his	JAUA
ile thr AUU ACU	val GUG	leu CUC	2,5	pro	Sy r	leu his asm his CUG CAC AAC CAC	าอกว
ile Auu	1 glu v G GAG G	p trp le c UGG CL	0 r 0	phe UUC C	ser UCU	his CAC	SCUCC
thr	va1 GUG	a s p G A C	arg AGA	phe uuc	91y GGC		ACC
Jeu	a s p G A U	gln CAG	91y 66c	asp GAC	asn AAU	91y 66c	ວກວເ
250 val GUG	280 a s p G A U	310 his CAC	340 1ys AAA	370 thr ACA	400 thr ACG	430 91u 6AG	CUA(
asp GAU	val GUA	met AUG	thr Acc	ile AUA	asn AAC	his CAU	3ACA(
1ys. AAG	phe UUU	11e AUC	1 y s AAA	met AUG	met AUG	leu UUA) n n n
pro lys pro cca aag ccc	trp UGG	970 000	ser UCC	cys UGC	ile AUC	ser val ucu gug	AGGA(
1ys AAG	ser AGC	glu leu GAA CUU	11e AUC	thr	020	ser ucu	:UAC/
	phe UUC		thr ACC	leu CUG	gln CAG	cys UGC	3600
010	gln CAG	ser AGU	1ys AAA	ser AGU	thr	thr	UGGAGCCCUCUGGUCCUACAGGACUCUGACACCUACCUCCACCCCUCCCU
phe uuc	val GUC	val GUC	g]u GAG	val GUC	asn	phe UUC	4600
11e AUC	g]u GAG	ser UCA	11e AUC	lys AAA	1 y s A A G	thr ACU	1990

INVENTOR(S): CABILLY ET AL. **APPLICATION SERIAL NO: 07/205,419 SHEET 10 of 19** Xbal EcoRI EcoRI 靊 BamHi Pstl Hpall Pstl Sau3A BamHi pHGH **Aval** Note Sall p x 17G4 Ap^R 207-1* Ava II Aval Pstl ApS Pst I, Ava II Isolate 333 bp fragment Anneal primer 5'p ATGACAT TGTGATG Klenow Pol I + 4 dNTP's EcoRI Klenow Pol I + 4dNTP's BamHI BAP Isolate large vector Sou3A fragment Sau3A T4 DNA ligase Hpall Sou 3A Sall Pst I Isolate kappa fragment Psti Ava II partial p & CEAInti Klenow Pol I + 4 dNTP's Hpa II Isolate 490 bp fragment ApR Ava I Ava I, Xba I Isolate 1240bp fragment Klenow Poll + 4dNTP's Xbo I BAP Hpall isolate 169 bp Xba I, Hpa II fragment Isolate large vector fragment T4 DNA ligase Xbal Hpall EcoRi BamHI 1000 Sall Ava II Psti Psti TcR pBR322 pxCEAInt2 (XAP) ApR Apf Avo I **EcoRI** Ava I Klenow Pol I + 4 dNTP's Klenow Pol I + 4 dNTP's Pst I Pstl Isolate KCEA Isolate large vector fragment fragment T4 DNA ligase Xbal Hpall Avall Psti PACEA EcoRI trp207-1* ApR BomHI (XAP) Sali

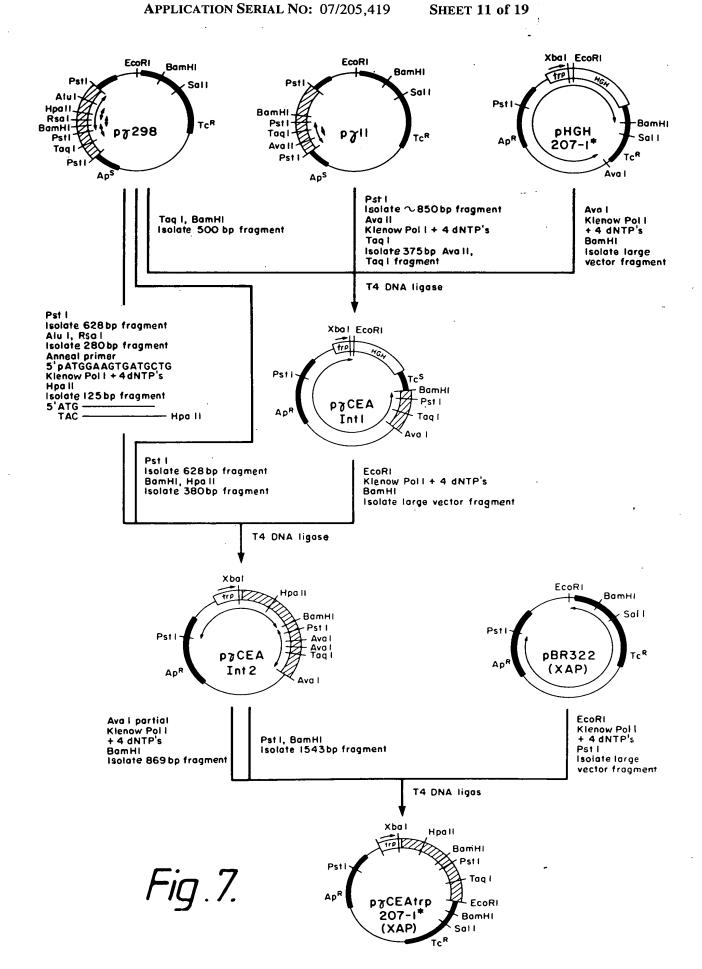
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RECOMBINANT IMMUNOGLOBULI

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PRE RATIONS

APPLN. FILING DATE: JUNE 10, 1988
TITY: RECOMBINANT IMMUNOGLOBULY
PRESENTATIONS
INVENTOR(S): CABILLY ET AL.



APPROVED O.G. FIG.

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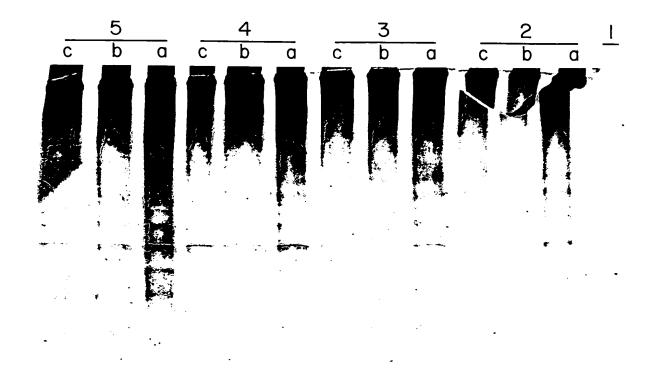
DRAFTSMAN

APPLN. FILING DATE: JUNE 10, 1988
TITLE RECOMBINANT IMMUNOGLOBULIDE PRESERVATIONS

INVENTOR(S): CABILLY ET AL.

APPLICATION SERIAL No: 07/205,419

SHEET 12 of 19



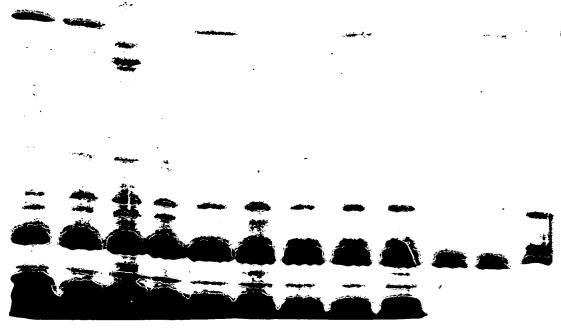
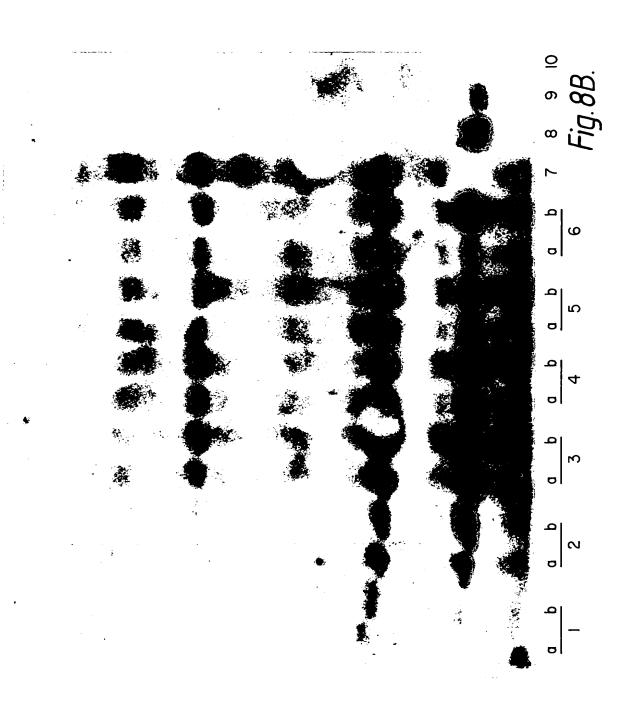


Fig. 8A.

APPROVED O G. FIG. 3¥ DRAFTSMAN

APPLN. FILING DATE: JUNE 10, 1988
TITE: RECOMBINANT IMMUNOGLOBULE
PROARATIONS
INVENTOR(S): CABILLY ET AL.
APPLICATION SERIAL NO: 07/205,419
SH

SHEET 13 of 19



APPLN. FILING DATE: JUNE 10, 1988
TITLE RECOMBINANT IMMUNOGLOBULIN
PREPARATIONS
INVENTOR(S): CABILLY ET AL.
APPLICATION SERIAL NO: 07/205,419
SHE

CLASS SUBCLASS

APPROVED O.G. FIG.

DRAFTSMAN

SHEET 14 of 19



2 5 6 8 Fig.8C.

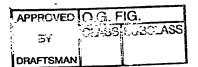
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TITLE: PECOMBINANT IMMUNOGLOBULIN

DRAFTSMAN INVENTOR(S): CABILLY ET AL.

APPLICATION SERIAL NO: 07/205,419 SHEET 15 of 19

30ng 70ng 0.10µg anti-CEA 0.30µg anti-CEA 1.00µg anti-CEA 1.00



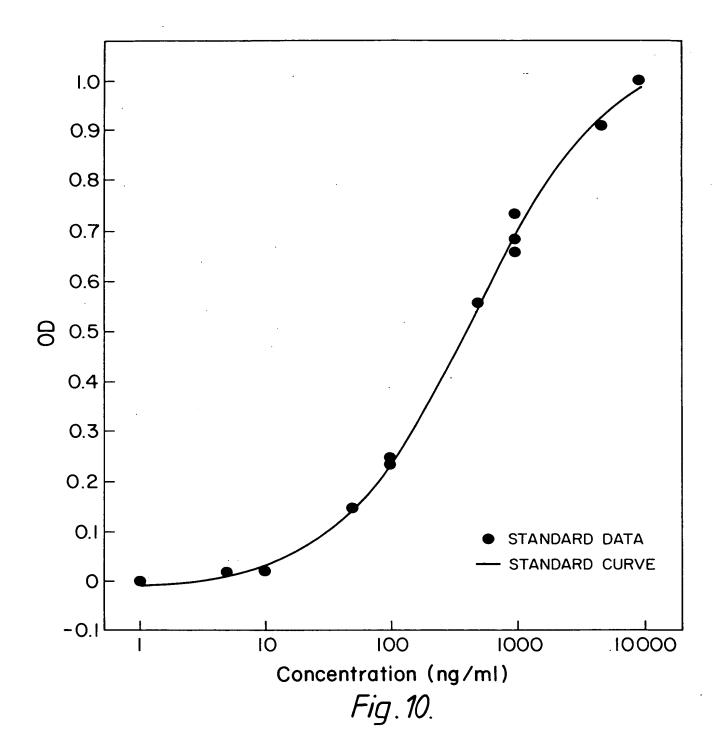
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TITE: RECOMBINANT IMMUNOGLOBUL
PR. ARATIONS

INVENTOR(S): CABILLY *ET AL*.

APPLICATION SERIAL NO: 07/205,419

SHEET 16 of 19



APPROVED O G. FIG.

5Y CLAUS SUBCLASS

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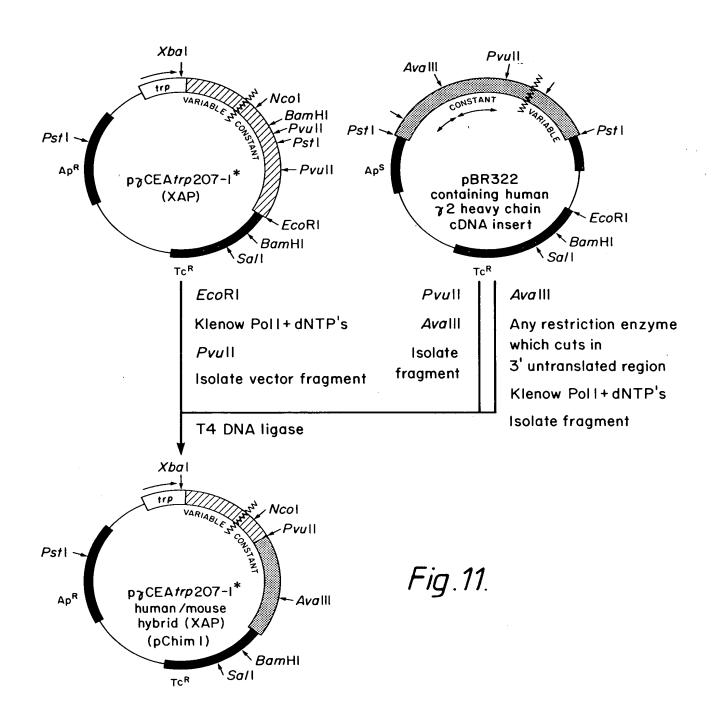
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TITE: RECOMBINANT IMMUNOGLOBUL

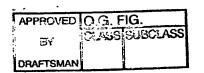
PR. ARATIONS

INVENTOR(S): CABILLY ET AL.

APPLICATION SERIAL NO: 07/205,419

SHEET 17 of 19



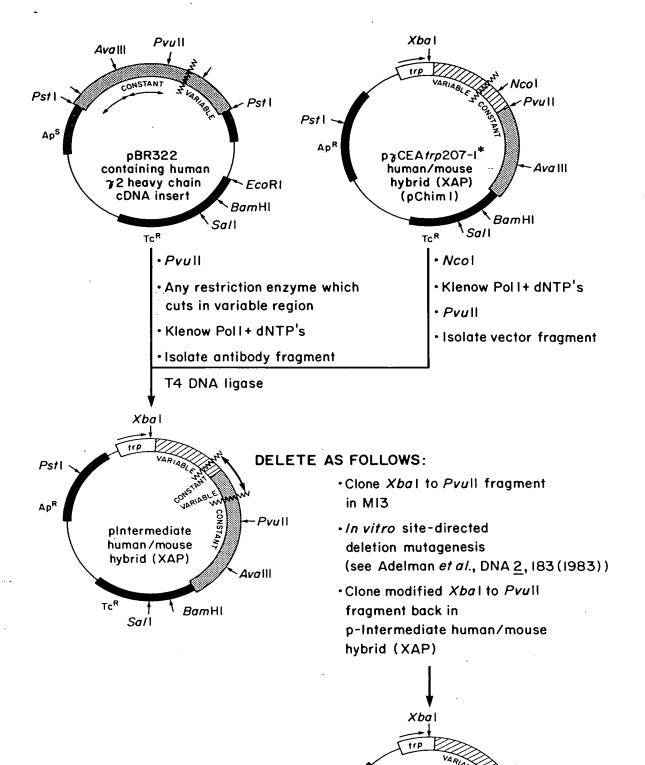


APPLN. FILING DATE: JUNE 10, 1988
TYPE: RECOMBINANT IMMUNOGLOBUTE
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SHEET 18 of 19



Pst I

 Ap^R

pyCEA*trp*207-1 human/mouse

hybrid (XAP) (pChimII)

Sall

Pvull

Avalli

BamHI

Fig.12.

